## III. Remarks

The undersigned gratefully acknowledges with appreciation the Examiner's withdrawal of the obviousness-type double patenting over claims 1-13, 18-19, 21-22, 25-29, 31-47, 76-77, and 80 of copending Application No. 09/435576 and the Examiner's withdrawal of the rejection of claims 76-87 under 35 U.S.C. 103(a) over Alberts et al. (U.S. Patent No. 4,997,658).

The specification has been amended to properly recite the priority claim of the present application.

### A. Status of the Claims

Claims 76-84 and 88-89 are pending in this application. Claim 76 has been amended without prejudice, incorporating the Tmax range recited in previous claim 87. Claims 85-87 have been cancelled without prejudice. New claims 88 and 89 have been added. Support for newly added claims 88 and 89 can be found in the specification as originally filed at page 20, lines 3-6. It is respectfully submitted that no new matter had been added by virtue of these amendments.

### B. Rejections under 35 U.S.C. § 103

#### 1. Chen et al. (5,837,379)

The rejection of Claims 76-87 over U.S. Patent No. 5,837,379 to Chen et al. was maintained. In the Office Action, the Examiner again stated that "[i]t is deemed obvious to one of ordinary skill in the art at the time the invention was made to look to the guidance provided by Chen et al. and include the instant lovastatin in the controlled release dosage form. One would be motivated to do so since Chen teaches a variety of medicaments that would benefit from the use of the instant controlled release formulation and teaches the instant active as one of the suitable medicaments. Therefore, one could reasonably expect similar results by including lovastatin in Chen's controlled release device."

"Furthermore, it is the Examiner's position that the instant controlled release device would meet the instant functional limitations since Chen's controlled release device is similar in structure and formulation to applicant's dosage form described in the specification; in particular Table 1. Therefore, it is the examiner's position that both would function similarly if not the same since the structures of the instant invention and that of the prior art are the same."

This rejection is traversed. The Chen et al. '379 patent is directed to controlled release dosage forms and incidentally mentions lovastatin in an exhaustive list (see column 2, line 51 to column 3, line 11 of Chen et al.) of over one hundred possible agents including various classes of drugs and specific drugs in multiple forms (e.g., salts, esters, etc.)

Applicants respectfully submit that one skilled in the art would not be motivated to select the particular claimed species (i.e. lovastatin) from the large genus disclosed at column 2, line 51 to column 3, line 11 of Chen et al. In support of this position, it is respectfully submitted that with respect to Chen et al., (i) the size of the genus is not sufficiently small as to render each member of the genus inherently disclosed, (ii) the reference does not expressly teach a particular reason to select the claimed species; and (iii) there is no teaching of structural similarity in the reference. See MPEP 8th Edition, 2nd revision 2144.08 II (A)(4)(A-C). A discussion of these points follows:

**(i) The size of the genus is not sufficiently small as to render each member of the genus inherently disclosed**

The fact that a claimed species is encompassed by a prior art genus is not sufficient by itself to establish a *prima facie* case of obviousness. *In re Baird*, 16 F.3d 380, 382, 29 USPQ2d 1550, 1552 (Fed. Cir. 1994). Some motivation to select the claimed species or subgenus must be taught by the prior art. See e.g., *In re Deuel*, 51 F.3d at 1558-59, 34 USPQ2d at 1215.

It is respectfully submitted that the size of the possible active agents which can be used in accordance with Chen et al. is sufficiently large as not to inherently disclose each and every individual species (e.g. lovastatin) which falls within their broad genus.

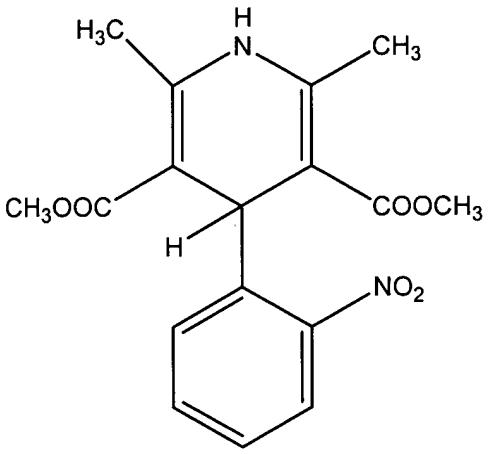
**(ii) The reference does not expressly teach a particular reason to select the claimed species**

If a prior art reference expressly teaches a particular reason to select the claimed species, the Examiner should point out the express disclosure which would have motivated one of ordinary skill in the art to select the claimed species. See MPEP 8th Edition, 2nd revision 2144.08 II (A)(4)(B). It is respectfully submitted that the only recitation of lovastatin in Chen et al. is embedded within a large genus. Accordingly, the Chen et al. reference does not expressly teach a particular reason to select lovastatin from the plethora of other possible species in the genus of the reference.

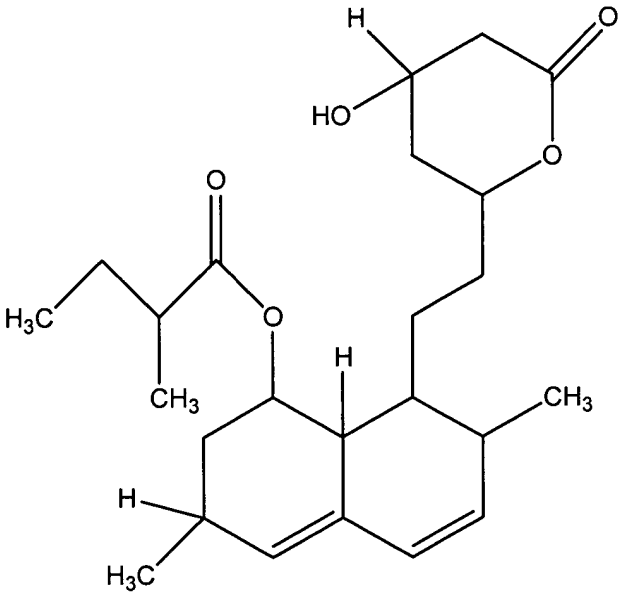
**(iii) There is no teaching of structural similarity in the reference**

If a preferred species is structurally similar to that claimed, its disclosure may motivate one of ordinary skill in the art to choose the claimed species from the genus. See, e.g., *In re Dillon*, 919 F.2d at 693, 696, 16 USPQ2d at 1901, 1904. It is noted that the preferred active agents exemplified in Chen et al. is nifedipine in Examples 1 and 2.

It is respectively submitted that nifedipine is not similar in structure to lovastatin and does not provide similar pharmacological activity. Nifedipine is a calcium channel blocker which is used primarily for the treatment of hypertension, while lovastatin is an HMG COA reductase inhibitor for the treatment of hypercholesterolemia. Structurally, nifedipine is a dihydropyridine compound and lovastatin is a lactone based structure. The structures of these compounds are set forth below in order to show the dissimilar structures of these two agents:




Nifedipine




Lovastatin

Accordingly, as Chen et al. does not teach any preferred species which have structural similarity to lovastatin, there is no motivation therein to one skilled in the art to select lovastatin from the large genus disclosed therein.

Further, any teaching or suggestion in the reference of a preferred species that is significantly different in structure from the claimed species weigh against selecting the later selected species. See, e.g., *In re Baird*, 16 F.3d 382-83, 29 USPQ2d 1552 (Fed. Cir. 1994). Accordingly, the examples of Chen et al. directed to a compound (i.e. nifedipine) that is not structurally similar to lovastatin (as discussed above) is further evidence that one skilled in the art would not be motivated to select lovastatin from the genus described therein.

The Examiner takes the further position that Table 1 of the present application is similar in structure to the formulations of Chen et al. and that both would function similarly, if not the same. Applicants respectfully disagree with this position. The broad ranges described in the specification at Table 1 provide guidance to one of ordinary skill

in the art to prepare a dosage form of the present invention with routine experimentation. One skilled in the art would appreciate that lovastatin formulations could be prepared that do not meet the limitations of claim 1, but would generically fall with the ranges of Table 1 of the present application.

Applicants respectfully submit that Chen et al. fail in the very least to teach, hint or suggest the $T_{max}$ range recited in the present claims as no information is provided in the reference concerning a desired time to maximum plasma concentration (Tmax) for any drug, let alone lovastatin. Further, there is no statement in Chen et al. relating to Tmax, and there is no suggestion in Chen et al. that a particular Tmax would be desirable for controlled release formulations containing lovastatin.

Applicants further submit that Chen et al. fail to teach or suggest a controlled release oral solid dosage form which increases the bioavailability of an active agent as compared to the same amount of the active agent administered in an immediate release form as recited in independent claim 76 (with respect to lovastatin). In addition, there is no information contained in Chen et al. regarding any pharmacokinetic values with respect to lovastatin, nor is there any mention of lovastain acid in Chen et al.

Therefore, Applicants respectfully submit that it is only with the benefit of the disclosure of the present application, that one skilled in the art would be motivated to prepare a formulation that (i) increases the bioavailability of lovastatin and does not increase the bioavailability of lovastatin acid, as compared to the same amount of lovastatin administered in an immediate release dosage form and (ii) provides a time to maximum plasma concentration (Tmax) at from about 10 to about 32 hours. Accordingly, the Examiner is using impermissible hindsight reasoning in making this rejection.

Therefore, it is respectfully submitted that the Chen et al. do not teach or suggest the presently claimed invention and the Examiner is respectfully requested to withdraw the obviousness rejection over the Chen et al. reference.

**2. Cheng et al.**

Claims 76-86 were again rejected under 35 U.S.C. 103(a) "as being unpatentable over the Cheng et al., Evaluation of Sustained/Controlled Release dosage forms of 3-Hydroxy-3-Methylglutaryl-Coenzyme A(HMG-CoA) Reductase Inhibitors in Dogs and Humans, Pharmaceutical Research (1993), 10:1683-1687. . . ."

In the Office Action, the Examiner indicated that "[t]he rejection of claim 87 is withdrawn."

Although Applicants disagree with the Examiner's rejection of claims 76-86, for purposes of advancing the prosecution of the present application, independent claim 76 has been amended without prejudice to incorporate the Tmax range of claim 87.

Accordingly, it is respectfully submitted that the rejection of the present claims over Cheng et al. is now moot andthe Examiner is requested to withdraw the obviousness rejection over Cheng et al.

**C. Double Patenting Rejections**

Claims 76-87 were rejected for obviousness-type double patenting over claims 1-12 of U.S. Patent No. 5,916,595 and 6,485,748.

**1. U.S. Patent Nos. 5,916,595**

In response to the obviousness-type double patenting rejection over claims 1-12 of U.S. Patent No. 5,916,595, a terminal disclaimer over this patent is filed herewith.

Applicants note that the obviation of an obvious-type double patenting rejection by the filing of a terminal disclaimer is not an admission, acquiescence, or estoppel on the merits of an issue of obviousness. *See Quad Environmental Technologies Corp. v. Union Sanitary District*, 946 F.2d 870, 873-74, 20 U.S.P.Q.2d 1392, 1394-95 (Fed. Cir. 1991).

**2. U.S. Patent Nos. 6,485,748**

The rejection of claim 76-87 over claims 1-12 of U.S. Patent No. 6,485,748 is traversed. Applicants note that when considering when the invention defined in the claim of an application is an obvious variation of the invention defined in the invention of a patent, the disclosure of the patent may not be used a prior art. However, the specification can be used as a dictionary to learn the meaning of a term in the patent claim, or be examined with respect to those portions which provide support for the claims (See MPEP 8th Edition, Revision 2, Section 804(2)(B)(1)).

It is respectfully submitted that the claims of the '748 patent patents fail in the very least to teach, hint or suggest the $T_{max}$ range recited in the present claims. Further, it is again respectfully submitted that the claims of the '748 patent fail to teach or suggest a controlled release dosage form comprising lovastatin wherein the dosage form increases the bioavailability of lovastatin and does not increase the bioavailability of lovastain acid, as compared to the same amount of lovastatin administered in an immediate release dosage form as presently claimed.

In view of the terminal disclaimer filed herewith with respect to the '595 patent and the arguments presented with respect to the '748 patent, the Examiner is respectfully requested to remove these obviousness-type double patenting rejections.

## IV. Conclusion

It is now believed that the above-referenced rejections have been obviated and it is respectfully requested that the rejections be withdrawn.

It is believed that no fee is due for this response. If it is determined that any fee is due, the Examiner is specifically authorized to charge said fee to Deposit Account No. 50-0552.

An early and favorable action on the merits is earnestly solicited.

Respectfully submitted,
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